TECHNOLOGY PHARM
USU’s Heady Agricultural Biotechnology Environment

by Douglas Steel
Wasatch Digital iQ - October 2001

In the areas of genetics, genealogy, and biomedical research in Utah, Salt Lake City and the University of Utah usually receive most of the recognition. The truth of the matter, however, is that developments in the confluence of these areas are still probably years away from widespread commercial applicability and products that will benefit the human condition.

Conversely, the field of agricultural biotechnology (Ag/Bio) is years ahead of the human counterparts, with products already in development and coming to market. Progress in Ag/Bio has the potential to affect the lives of every person on the planet: by increasing the available food supply, providing new drugs, transplant tissues, and vaccines at a breakneck pace; safeguarding the security of our foodstuffs; and leading the way in cloning technology.

To be a leader in this emerging field, an institution needs to have the commitment, persistence, expertise, and resources of a world-class agricultural R & D facility, along with the biotechnology infrastructure and skills of molecular biology and bioengineering, in an environment that fosters collaboration and joint ventures.

Utah has one of the top institutions in the world for these endeavors, with the aforementioned combination of skills and resources, directed by a group of committed leaders. The place is Utah State University (USU) in Logan, just 90 miles from the front doors of the "other" genetics experts.

A SHORT HISTORY LESSON

Utah State University has a long history in the agricultural sciences, originating as the Agricultural Experiment Station at a time when technology's leading edge was developing the best design for a plow blade. USU was one of the original "Land Grant" institutions in the United States, endowed by the Federal Government to provide education, research, and outreach services to farmers.

The intention of the Land Grant program was to ensure the growth and prosperity of the American food supply and agricultural sector during an era when a significant percentage of Americans were either farmers or grew up on farms. Today, less than 2 percent of the population provides the food for America and much of the world.

Since its beginnings, USU has not only kept pace, but has remained on the forefront of scientific and technological innovation. To date, for example, USU has put more experiments on space shuttle flights than any other school in the country.

In the late 1980s, as biotechnology was emerging as a commercial industry, USU began exploring how to become a player in this field, despite being smaller and less well known than other universities. Their solution was to create a centrally available Biotechnology Center that would provide faculty and staff with all the resources they needed for research, avoiding unnecessary overlap and duplication of services.

"This was probably the first time in Utah history that all the agriculture entities in the State agreed and presented a united front to the State legislature to seek funds for the Center", says H. Paul Rasmussen, director of the Agricultural Experiment Station at USU, which includes the Biotechnology Center.

The Center was funded by the State, with additional funding from the US Department of Agriculture. This pooling of State and Federal funds has had a lasting effect on the attitude toward biotechnology at USU, making it almost synonymous with agricultural applications and interests.

"We recognized even back then that if we were going to be successful growers, in the future we would have to find ways to enable plants to defend themselves, and not continue to rely on pesticides," says Rasmussen. Today, all the departments in the College of Agriculture (Nutrition and Food Science and Economics; Plants and Soils and Biometeorology; Animal, Dairy, and Veterinary Science; and Agriculture Systems Technology and Education)--as well as departments in other colleges, including Biology and Natural Resources--benefit from this arrangement.

With this in mind, USU implemented a second initiative: to hire faculty with interests and skills in biotechnology. Over time, the school has built a solid team of investigators around the core facilities. Says Rasmussen, "I think Utah is unique in having agriculture and biotechnology as tightly linked as they are, academically and politically. This is a strong partnership, but we need to do a better job of getting the products of our research out into the private sector, to the growers and farmers, and all the way to the fork."

USU president Dr. Kermit Hall stresses other reasons Ag/Bio is critical to the future of Utah's high tech economy. "Plant and animal genomics research is central to making human genomics work. The models developed in mammals are relevant to humans, yet you can do things with animals that you could never try in humans. In terms of plants, Utah doesn't have much of a pharmaceutical industry base; plant genomics offers us the chance to get into that business, by engineering plants to produce drugs."

THE CENTER OF ACTIVITY

The Biotechnology Center receives line item funding from the State legislature, as well as support from grants and contracts. It began as one of the Centers of Excellence, then evolved beyond that program.

The Center has three overlapping missions: to operate the Center resources as a service for investigators in any department on a contract basis; to manage its own research program for scientists who are housed in the Center; and to provide education through outreach initiatives.

The Center also conducts contract research for outside institutions. "We believe if we can develop a skilled biotechnology workforce in Utah, we might be able to attract regional branches of the large biopharmaceutical companies," says Dr. Kamal Rashid, acting executive director for education and outreach for the Biotechnology Center, "especially with the looming shortage of biotech workers.

"Once we have the labor force, it will be a selling point for companies to move here."

The Center has been aggressively marketing itself inside the State as well, attracting top high school science students to its Biotechnology Summer Academy, an intensive five-day training and internship program. It also has plans in conjunction with Salt Lake Community College to develop a training curriculum for public school teachers in Utah.

In addition, the Center has established a national reputation for its program to train technologists in Bioprocessing, the technology of manufacturing products through DNA and protein manipulation.

"When the biopharmaceutical companies decide where to send their people for training, it always comes down to MIT, Penn State and Utah State," says Rashid, "and they come from all around the country." It is more cost-effective for companies to outsource their training through programs such as Utah State's, and the strict requirements for training and retraining imposed by the FDA ensure that the programs will continue to receive students and generate money. “It's a multi-billion dollar industry,” says Rashid.

The Center provides a number of services for faculty and outside companies, overseen by Dr. Tom Grover. The facility is equipped to produce monoclonal and polyclonal antibodies, sequence DNA, perform mass spectrometry analysis, sequence and purify peptides and proteins; and culture bacteria and cell lines in bulk.

"These are services that often aren't readily available together on a commercial basis," says Grover, and the list of clients spans the campus and the country. “We have a very well trained staff and are known for the advice and help we provide, not just the services."

FROM THE BENCH TO THE MARKET

One benchmark of the effectiveness of an Ag/Bio program is the ability to commercialize the technologies developed in-house. Historically, USU has created more varieties of named and released small grains (such as barley, oats, and wheat) than anywhere else in the West.

"This tradition will continue as we genetically engineer new forms of small grains and license these technologies,” says Rasmussen. “We are also expanding into the genetic engineering of animals, developing dipstick tests that track their health, and pushing a new initiative we call ‘Agro-security' to ensure the safety of our food supply from natural or intentional contamination.”

The Center contributes to research and commercialization at companies in the State and around the country, ranging from startups such as Phytokinetics, Apomyx, and Echelon, to mature companies like Hyclone, and institutions including the Albert Einstein School of Medicine in New York and the Centers for Disease Control in Atlanta. In addition, says Rashid, “if we feel that research has potential for commercialization, we can perform feasibility studies and help them get started. This has already happened five or six times."

Part of what makes such commercialization possible is the sheer mass of research conducted at USU. “The University makes about $125 million annually in research grants, says Grover. “We are known for Biotechnology and Space Science Research.”

Remaining strong, he adds, will require staying at the cutting edge of new technologies. “We are branching out into proteomics, bioinformatics, and genomics, in training people and providing research services, while remaining strong in our existing competencies.”

HERE TODAY, CLONED TOMORROW

One USU Ag/Bio research star is Dr. Ken White, professor of Reproductive and Embryo Biology since 1991. The research in his labs has three main emphases. One is the creation of transgenic animals (mice, rabbits, and goats). Such animals have either a genetic modification that allows them to produce a medically useful substance like interferon (which can be isolated and purified for use as drugs), or a molecular defect that makes them a useful model for a particular disease state.

“The next generation of drugs that you and I take are going to be based on proteins that the body already makes, but in insufficient quantity,” says White. “We can make up the shortfall through transgenic production.”

Another research area for White is the process of egg activation: how fertilization results in a viable embryo. In addition to answering many questions and solving many problems of human production, discoveries in this area are considered crucial to the eventual success of attempts at cloning.

His most prominent area of investigation right now is mammalian cloning. Prior to 1997, when Dolly the Sheep arrived in the world, White and others were trying to clone using embryonic stem cells. Dolly, the first living demonstration that clones could be created from any type of cell in the body, changed everything.

Recently, White and other colleagues have been working with a company called XY Genetics to preselect the type of animal they want to create—"whether for milk production, meat quality, or some other economic characteristic," he says.

They then take a tissue sample from the animal and grow the cells in a test tube until they have millions of copies of those cells, and freeze them away in storage.

The next step is to extract the DNA from the frozen cells and inject it into the unfertilized eggs of cows, generate embryos, then implant those embryos back into cows and wait through gestation to obtain a potentially unlimited number of identical animals.

White envisions being able to select cows with high milk production and cloning them, creating a line of cattle that produce 50,000 pounds of milk per year, instead of 15,000 pounds.

This technology, however, is not a slam dunk. First, the researchers will have to wait months to know whether they have been successful. Furthermore, only about 10 percent of embryos will go successfully to term.

White believes the rewards of the procedure outweigh the risks. "This is the future of how pharmaceuticals will be produced," he says. "Many drugs would never be economically viable or safe for human use if they had to be extracted from cadavers the way insulin or Human Growth Hormone used to be. Using transgenic and cloning technologies, we can use the animals as living 'bioreactors' and isolate the proteins from their milk."

THE SOCIETAL DEBATE

It is impossible to properly measure progress in Ag/Bio without also considering the wider social implications of current public policy issues--including cloning, the creation of genetically modified organisms (GMOs), and the use of organisms as living "bioreactors" engineered to produce pharmaceuticals or vaccines.

Researchers at USU are not afraid to take on the debate surrounding these topics. Rasmussen explains, "I think the public has a right to be concerned about GMOs, and they also have a responsibility to educate themselves about what really happens when an organism is modified. There are many GMOs that the public consumes every day that don't bother them in the least. Every time the Biotechnology Center comes up with a modified organism, the University has a responsibility to demonstrate the safety for consumption and to provide the public with materials to become educated."

White appreciates that cloning is a controversial topic to the public right now, but distinguishes it from the debate surrounding GMOs. "We are not doing anything to 'stir up' the makeup of an animal, just identifying genes that already exist and amplifying them in the population, making copies. It is no different from a case of identical twins."

LOOKING AHEAD

As the pace of scientific discovery accelerates, matched by the costs of commercializing these technologies, USU faculty members are optimistic about the future. "We are going to continue our education and outreach activities, trying to reach more and more students and teachers," says Rashid.

Grover and Rasmussen both note that equipment now becomes obsolete roughly every six years, and it is very expensive to stay current. "Our greatest need is to keep up with technology," says Grover. Rasmussen adds, "We also need to attract faculty trained in the newest techniques, to match salaries and provide the resources to bring these people here and hang on to them."

White looks ahead to what we can expect from the discoveries of the next 5 to 10 years: "In 5 years we will be generating 'designer animals' with specific traits. I think we will be saving cells so that we can clone them if they die. We will be engineering animals to be more disease resistant, or to produce pharmaceuticals and nutriceuticals. I think we are not far off from delivering vaccinations in Third World countries via drinking a bottle of milk. Another important area is in endangered species preservation."

In research that sounds like science fiction, White is already experimenting with cloning using the DNA from the Argali, an extremely rare Tibetan sheep.

Hall lends his own perspective on biotechnology: "I am crazy enough as a humanist to think the future is going to be biological, and not electronic. Electronics is going to become the servant of biology. Agricultural biotechnology has the potential to directly affect the economic future of the state of Utah.

"We can't afford to miss this opportunity! The people in Oregon aren't missing it, nor in Idaho or California, or even in Wyoming. We can't think of technology as just about silicon wafers. The future of computing is not in silicon, it is molecular. As we move toward nanotechnology, we are approaching the function of biological systems and applying that commercially. We are talking about computers 250 million times faster than the fastest computers today. Does Utah want to be a part of this future, or see our talent being exported to Wyoming?"

SIDEBAR: THE USU CENTER FOR GENOMIC RESEARCH INITIATIVE

At the request of Utah State University President Kermit Hall, Dr. Noelle Cockett, Professor in Animal, Dairy and Veterinary Sciences, is directing an advisory committee of faculty members to develop a major USU Center for Genomics Research (CGR).

Hall observes that the State of Utah "has a significant deficit in the technology associated with plant, animal, and native species genomics. There is a disconnection between the richness of university research in these areas and the translation of that into business innovation."

Cockett, a nationally-recognized genomics researcher investigating genetic markers in economically-important livestock, is also the US coordinator for the identification of DNA markers for the worldwide sheep genome project.

Once established, the CGR will coordinate research activities involving:

- biodiversity in agricultural and natural populations of plants and animals, leading to regulation of the balance of native to wild species, control of invader species, and conservation of germ plasms;

- microbial genomics, resulting in the creation of new industries including bioremediation, pharmaceuticals, and food safety; and

- application of genomic, proteomic, and bioinformatic technologies to improve the efficiency of agricultural production.

It is expected that the CGR will significantly enhance the University's ability to obtain research funding, recruit and retain high level faculty and students, and strengthen collaborations across departments in the sciences, agriculture, and engineering.

Hall notes, "Today in biotechnology, proteomics, genomics, and bioinformatics, the opportunities for employment of graduates is shooting off the scale, yet we are not producing enough of those people. If

we don't ratchet it up, we will miss a significant opportunity to grow the state's economy and to help students.

"There is a clear link between what the Governor is trying to accomplish in Silicon Valley and what can be done in the Cache Valley. The wafer chip and the test tube can cross paths right here."

At present, the committee is developing the model for the Center, selecting member faculty, identifying funding sources for the facility's creation and ongoing support, and setting funding priorities. Hall has indicated that the task force will be prepared to present a "foundation" for the CGR later this fall.